Speaker: Dr. Kaihang Wang, University of Cambridge (UK)

Title: Rewriting Natural Decoding Rules by de novo Genome Synthesis

Abstract:

Unnatural amino acids could be incorporated to expand the chemical, physical and biological properties of proteins to expand the function of life itself. There are two conceptual possibilities to achieve this goal: i) creation of orthogonal decoding rules running independently to the wildtype decoding rules to incorporate unnatural amino acids; and ii) de novo synthesis of a new genome with artificially redefined synthetic decoding rules to expand natural decoding capacities to include unnatural amino acids.

To explore the first possibility, the orthogonal ribosome and multiple tRNAs were co-evolved to efficiently decode cognate quadruplet codons on an orthogonal mRNA for incorporation of multiple distinct unnatural amino acids. This established the possibility to enhance the efficiency of unnatural amino acid incorporation in response to a synthetic orthogonal quadruplet codes, creating maximally $4^4=256$ new quadruplet codons for unnatural amino acid incorporation.

The second possibility requires the de novo construction of a synthetic genome with re-programmed synthetic decoding rules to re-build a synthetic life that fundamentally go beyond the limits of the 20 natural amino acid side chains. To pave the foundation to reach for this goal, an efficient, specific, and iterative method in E. coli to replace defined genomic fragment with synthetic sequence (replicon excision enhanced recombination, REXER) has been developed; together with a feasible, modular, and scalable route for de novo genome synthesis (genome stepwise interchange synthesis, GENESIS), which allows the replacement of the entire 4.6-mb E. coli genome with synthetic DNA in around 15 or less iterated REXER steps.
Speaker: Dr. Simon Ausländer, ETH Zürich (Basel campus, CH)

Title: Engineering of Mammalian Cell Control Systems Based on Gene Switches & Circuits

Abstract:
Synthetic gene switches are genetically-encoded biosensors that provide mammalian cells the ability to specifically detect biomolecules and in response fine-tune protein expression levels in an input-output relationship. Especially the design of gene switches responding to disease-related input molecules in the physiological concentration range offers great opportunities for cell-based biomedical applications. Customized mammalian cell lines engineered with such gene switches can be implemented into diagnostic tests to monitor diseases by quantifying specific blood-derived biomarkers. When microencapsulated and implanted into mice, engineered cells can also be used in cell therapy in order to autonomously detect disease states and produce a therapeutic response.

The next generation of engineered cells will advance from one-input to multi-input signal integration transforming cells into sophisticated decision-making systems capable of performing complex information-processing tasks. Biological components, such as gene switches, are connected to each other to build gene circuits that are programmed by a set of different input signals for higher-order gene expression control in human cells. Post-transcriptional RNA controllers, cell-cell communication systems and 3D cell culture setups are new approaches that facilitate the design of large and complex gene circuits. In future, engineered cells will have the ability to logically respond to various disease-relevant input molecules at the same time thereby increasing the diagnostic precision as well as therapeutic intervention portfolio.
Speaker: Dr. H. Courtney Hodges, Stanford University (USA)

Title: New Approaches to Detect Dynamic Epigenetic Deregulation in Cancer

Abstract:
Epigenetic mechanisms, which regulate gene expression independently of DNA sequence, are critical for multicellular development and normal function. In the last decade, advances in cancer biology have revealed that epigenetic deregulation is a hallmark of malignancy. We have taken a special interest in BAF (mSWI/SNF) ATP-dependent chromatin remodeling complexes, which we found are the most frequently mutated chromatin regulators in cancer. Emerging evidence shows that BAF complexes contribute to hundreds of thousands of new cancers each year. Unfortunately, the mechanisms that drive pathogenic gene expression remain uncertain due to limited techniques to detect BAF cell-specific functions. Thus, there is an urgent need for new assays to probe their contribution to malignancy. Here I will describe the common mutations of BAF subunits that alter gene regulation in cancer, and summarize their effects on the epigenetic landscape. I will also describe our quantitative approaches to uncover new mechanisms and dynamics of remodeling in living cells. Many questions remain regarding the physical and systems-biological mechanisms of these and other epigenetic systems, and how they should be targeted for therapies. The widespread nature of epigenetic deregulation in different disease settings suggests that new technologies, including single-molecule and single-cell approaches, will yield many opportunities to improve detection, monitoring, or precision treatments of epigenetic disorders.
Speaker: Dr. Alejandro Ocampo, Salk Institute for Biological Studies, La Jolla, CA (USA)

Title: Epigenetic Reprogramming of Aging and Disease

Abstract:
Epigenetics has recently emerged as one of the most important mechanisms for the regulation of gene expression and cellular function. In addition, epigenetic changes induced by our lifestyle and the environment play crucial roles in human diseases as well as aging. For these reasons, therapeutic strategies aiming at the manipulation of the epigenome are been developed for the treatment of multiple diseases including cancer. I have recently demonstrated that epigenetic reprogramming by short-term expression of Oct4, Sox2, Klf4, and c-Myc (OSKM) also known as the Yamanaka factors can ameliorate hallmarks of aging in mouse and human cells. Interestingly, OSKM in vivo cyclic expression in a mouse model of premature ageing improves age-associated phenotypes in multiple organs and prolongs lifespan. Lastly, in vivo cellular reprogramming enhances the recovery of physiologically aged mice from metabolic disease and muscle injury. These observations highlight the importance of epigenetic regulation during mammalian aging and disease, and reinforce the potential of epigenetic reprogramming as a novel strategy for improving health and longevity.
Mini-symposium on Cancer Bioengineering  
room SV1717, EPFL, Lausanne, Switzerland, April 11, 2017

Speaker:  Dr. Carolina Tropini, Stanford University (USA)

Title:  Going with the Flow: a Multi-scale Approach to the Gut Microbiota during Osmotic Disturbance

Abstract:
The consortium of microbes living in and on our bodies is intimately connected with human biology. Unique for every person and dynamic over time, our microbiota is becoming an important facet of precision medicine. Despite incredible gains in describing this community, and emerging knowledge of the mechanisms linking it to human health, understanding the basic properties and responses of this ecosystem has been comparatively neglected. Most diseases have significant physical effects on the gut; diarrhea alters osmolality, fever and cancer increase temperature, and bowel diseases affect pH. Furthermore, the gut itself is comprised of localized niches that differ significantly in their physical environment, and are inhabited by different commensal microbes. Understanding the impact of common physical factors is necessary for engineering robust microbiota members and communities; however, our knowledge of how they affect the gut ecosystem is poor.

As a model of a biophysical perturbation, I am investigating how osmotic diarrhea affects the host and the microbial community. Osmotic diarrhea is extremely prevalent, caused by the use of laxatives, lactose intolerance, or celiac disease. In my studies I monitored osmotic diarrhea using a comprehensive and novel approach, which combined a mouse model with "omics" approaches, imaging, physical measurements, computational analysis and highly controlled microfluidic experiments. By bridging several disciplines from biology and physics, we developed a mechanistic understanding of the processes involved in osmotic diarrhea, linking single-cell biophysical changes to large-scale community dynamics. Our results indicate that physical perturbations can profoundly and permanently change the competitive and ecological landscape of the gut, with important health implications.
Sound can be music to please the ear, however the waves produced can be utilized as “Acoustic Tweezers” for the manipulation of cells and particles in a fluid medium. The acoustofluidics technology, combining sound waves with fluidics, becomes a revolutionary way to dexterously and noninvasively manipulate biological specimens. Firstly, this technique manipulates cells or particles using gentle mechanical vibrations. These vibrations create a pressure gradient in the medium to move suspended micro-objects yielding a contamination-free, contactless, and label-free manipulation. Secondly, acoustofluidics has minimal impact on cell viability and function. Thirdly, this technology can operate in a single micro-device without any external moving parts or complicated setups, which offer additional advantages in ease of use, versatility and portability. Here, we report a series of acoustic tweezers for the manipulation of micro-objects in a liquid medium or the microfluidic environment to address the problems in the field of biomedicine including tissue engineering, cell-cell interaction, disease diagnostics, and point-of-care-testing.
Mini-symposium on Cancer Bioengineering  
room SV1717, EPFL, Lausanne, Switzerland, April 11, 2017

Speaker: Dr. Alex Hughes, University of California, San Francisco, CA (USA)

Title: Inferring the Design Rules of Development by Tissue Reconstitution

Abstract:
The emergence of gut villi, the branching of the airway epithelium, and the wrapping and closure of the neural tube are all developmental transitions that convert flat tissue structures into more complex forms. I believe that a systems-level understanding of tissues sufficient to study their malfunction in disease will come through reconstituting their developmental transitions \emph{ex vivo}. I will describe our synthetic system for recapitulating the mechanics of mesenchymal condensation, a core vertebrate developmental program that encodes transitions in tissue complexity in diverse contexts. These efforts will enable fundamental studies on the interplay between tissue mechanics and morphogenesis, and instruct our efforts to bring developmental principles under engineering control for applications in basic science, regenerative medicine, and stimuli-responsive biological materials.